VAGINAL INFORMER APPLICATION FOR DELIVERY OF MICROARRAY PATCHES CONTAINING RILPIVIRINE FOR HIV PRE-EXPOSURE PROPHYLAXIS


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BACKGROUND

Health need

Studies of antiretroviral-based HIV pre-exposure prophylaxis (PrEP) have highlighted issues of user compliance with regimens that require daily dosing, particularly in low-resource settings (LRS). Longer-lasting contraceptive options could obviate compliance issues, but regular access to health care facilities for their administration remains challenging for many women. Longer-lasting and low-cost delivery methods that enable discreet self-administration have the potential to both improve user compliance as well as reduce the frequency of visits to a health care provider.

Technology solution

Vaginal delivery of dissolving microarray patches (MAPs) containing a sustained-release, nanoparticle formulation of rilpivirine holds promise for the self-administration of long-acting HIV PrEP. The discreet, easy-to-use form factor of MAPs may also increase user compliance.

Challenges and opportunities in product design

Designing a MAP to be delivered in the vagina (with dynamic and variable geometric, environmental conditions, and tissue characteristics) creates both design challenges. Alongside other early learnings, these challenges have underscored the value in pursuing patch and applicator development in parallel. Such concurrent product design allows features unique to one off-take (such as the patch’s geometry) to be informed by the other (such as the applicator’s ideal interface area), and vice versa (Figure 1).

Figure 1. Concurrent design informs requirements.

MAP development

Applicator development

Inform

CONCURRENT PRODUCT DESIGN

Functional requirements

Although rilpivirine MAPs remain in the early stages of development, and performance characteristics and specifications for them have yet to be fully determined, initial discussions and evaluation of desirable functional attributes (Table 1) that can be addressed by the applicator are helping inform the MAP’s design process.

Table 1. Functional attributes of MAP applicators.

Attribute

Description

Path Application: Physical

The ability of the applicator to prevent inadvertent delivery during the insertion process.

Path Application: Function

The ability of the applicator to promote accurate and possible delivery during the insertion process.

Force Application

The ability of the applicator to apply additional force to promote accurate delivery during the insertion process.

Ease of Use

The ability of the applicator to be used with minimal training.

Self-sterilization

The ability of the applicator to facilitate effective packaging of the MAP (e.g., under dry, low-heat, uncontrolled conditions) without the need for subsequent sterilization.

Patch Delivery

The ability of the applicator to deliver and separate from the MAP (a “core-in-plastic” delivery mechanism).

Surface Flatness

The ability of the applicator to result in minimal rigidity or thickness of the insertion as it leaves the applicator.

Package Condition

The ability of the applicator to store effectively the MAP (e.g., by preventing molecule loss or the formation of a dry crust that may obstruct delivery).

Disposal

The ability of the applicator to be definitively disposed of at the conclusion of the use cycle.

Cost

The ability of the applicator to be manufactured at a cost that does not exceed its USR value.

A FOUR-PHASE DESIGN PROCESS

Phase 1: Initial prototype development

To generate a breadth of applicator design approaches, we conducted multidisciplinary brainstorming sessions and interviews with subject matter experts in engineering, public health, commercialization, midwifery, and industrial design. These design approaches were consolidated into six main concepts (Table 2); initial prototypes were then constructed for a user study in South Africa that consisted of focus groups of potential users and conversations with local health care providers.

Figure 2. The two downselected applicator design concepts.

Phase 2: Preliminary downslection

Further downslection to two applicator design concepts (Figure 2) was informed by feedback from both the user study and preliminary assumptions of potential functional characteristics of the patch. In general, feedback from the user study centered on hygiene, discretion of the device, and similarity to current vaginal products.

Figure 3. Initial refinement of the downslected designs.

Phase 3: Final downslection and prototyping

A final round of prototyping of the digital and wand applicator designs is currently underway.

This phase seeks to explore specific design features aimed at addressing the functional requirements of the applicable tool. Only design concepts maximizing functionality and feasibility will move on to the design testing phase.

Phase 4: Design evaluation

In this upcoming and final phase, the applicator designs will be evaluated for their ability to reliably deliver the MAP into the vaginal mucosa. Testing will focus on verifying the key functional requirements and preliminarily validating the complete delivery process.

DESIGN EVALUATION

Verification

Applicator verification will test how key requirements can be met by the proposed applicator designs. Testing will also isolate these characteristics for individual evaluation—for example, a sled tester will assess the need for physical patch protection during application (photo).

Valuation

A vaginal model (Figure 4) has been developed to simulate testing environments and to assess the patch’s performance in the vaginal environment. This model is designed to both ergonomically simulate a common vaginal product (Table 1) as well as measure forces experienced by the MAP during application. Key learnings from developing this model are also informing patch-related development efforts.

Figure 4. Vaginal model.

Table 2. Vaginal model parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of canal</td>
<td>8 cm</td>
</tr>
<tr>
<td>Maximum canal width</td>
<td>5.2 cm</td>
</tr>
<tr>
<td>Maximum canal depth</td>
<td>3.0 cm</td>
</tr>
<tr>
<td>Intrabulbar pressure</td>
<td>~3.0 mm Hg</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>4.5 mg</td>
</tr>
<tr>
<td>Vaginal moisture tissue</td>
<td>Synthetic or excised</td>
</tr>
</tbody>
</table>

Although the work is ongoing, our user-centered process thus far underscores the value of concurrently developing a MAP and its applicator for vaginal delivery or any other route. From product ideation through to user studies, key learnings around the applicator, its functionality and potential utility for the end-user—plus appropriateness for the health care system and settings in which it will be used—will continue to inform and define design requirements for a MAP product that promises to be effective and discreet method for delivering longer lasting rilpivirine for HIV PrEP.

DECLARATION

Support for this project is made possible by the generous support of the American people through the United States Agency for International Development (USAID) under the terms of the Health Commodity Cooperative Agreement # AID-OAA-A-11-00051. The contents are the responsibility of PATH and do not necessarily reflect the views of USAID or the US Government.